

would enable VIA-FLIC measurements of the height of labeled positions in the ion channel.

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New Insights into the Membrane Mechanism of Action of Amphotericin B from Molecular Dynamics Simulations

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Amphotericin B (AmB) is a well-known polyene antifungal antibiotic that acts by forming channels in cell membranes. It is known that membrane sterols are essential for the AmB biological activity. The selective toxicity of AmB for fungal cells is attributed to the fact that it is more potent against fungal cell membranes containing ergosterol than against the mammalian membranes with cholesterol. There are two non-contradictory models suggesting what this may result from: either from stronger AmB-sterol interactions in case of ergosterol membranes or from a more appropriate environment for the formation of a functional pore provided by more ordered ergosterol-containing membranes.

To elucidate the molecular nature of the AmB higher selectivity for ergosterol-containing membranes than for cholesterol-containing ones, we used computational methods and studied (1) the AmB monomer insertion to membranes of different composition (containing or not 30% of ergosterol or cholesterol), (2) the formation of the putative AmB/sterol complexes in a lipid bilayer and (3) the formation of the AmB dimers in a lipid bilayer. To obtain the equilibrium description of these processes the free energy profiles were calculated for each of the studied systems. The significant differences in the affinity of AmB for different membranes have been found. The results indicate that the different behavior patterns of AmB in different membranes is sterol-dependent. The meaning of these differences for the mechanism of action of AmB and, more specifically, for the mechanism of channel formation in different membranes is discussed. The data obtained allowed us also to suggest a possible origin of the increased selectivity towards ergosterol-containing membranes of a novel class of less toxic AmB derivatives.

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STED-FCS on Near-Critical Lipid Membranes

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Dynamic phase separation in cell membranes is believed to play an important role in many membrane-associated cellular processes. This microheterogeneity is one of the reasons for anomalous diffusion of lipid molecules which is frequently observed in cell membranes. We have recently shown via Monte Carlo simulations that the presence of near-critical fluctuations in a lipid membrane may lead to transient anomalous diffusion of lipid molecules [1]. It is therefore extremely interesting to test, whether anomalous diffusion due to critical fluctuations can be observed experimentally in model membranes under appropriate conditions. We report results of our experiments on model lipid membranes exhibiting near-critical fluctuations using STED-FCS [2], an experimental technique which can provide valuable information on diffusion dynamics on spatial scales from a few tens to few hundreds of nanometers on time scales ranging from microseconds to seconds.

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Interactions of Lithium Ions with Lipid Membranes

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Lithium is a naturally occurring alkali metal which is very easily ionized to Li⁺, especially in aqueous solutions. Lithium is found mainly in mineral and seawater and in trace amounts in the human body. Lithium ions are being used in various fields ranging from energy storage to the treatment of mental illnesses including bipolar disorder and schizophrenia. The reason why lithium is such a peculiar ion is not exactly known except that its mode of interactions with charged surfaces depends on its hydration properties (i.e. interaction with nearby water molecules). We report two kinds of experimental measurements of lithium interactions with charged lipid membranes. One set of experiments involves X-ray scattering of multilamellar lipid vesicles in solution for which we measure how lithium salts modify van der Waals and electrostatic forces between neighboring membranes. The other set of measurements compare

the effect of added lithium on the activity of gramicidin channels in neutral and negatively charged lipid bilayers. We find that in both x-ray and channel measurements, lithium ions modify lipid interactions in a manner that differs from other monovalent positive ions.

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Superior Membrane Permeabilization and Solubilization Properties of Biosurfactants may be Explained by Heterogeneous Perturbation

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Biosurfactants such as antimicrobial lipopeptides, saponins, and bile salts often show a superior performance to permeabilize and lyse membranes and/or a better suitability for membrane protein solubilization than classical, synthetic detergents. We propose a classification of surfactants into those that are homogeneously disordering versus heterogeneously perturbing a given membrane to help explaining and predicting this behaviour. Typical synthetic detergents such as C12EO8, octyl glucoside, SDS, and lauryl maltoside were identified as homogeneously disordering by the limiting fluorescence anisotropy of several DPH derivatives reaching a characteristic, low level at the onset of solubilization. The biosurfactants surfactin, fengycin, iturin, digitonin, and lysophosphatidylcholine along with the synthetic CHAPS belong to another class that initiates membrane lysis without critical disordering the whole membrane. They disrupt the membrane locally due to a spontaneous segregation from the lipid and/or an ordering effect that induces packing defects. This may account for enhanced activity, selectivity, and mutual synergism of antimicrobial biosurfactants. They should also be prone to form partially-demixed, asymmetric micelles (or bicelles) with a relatively lipid- (and sterol?) rich core surrounding a solubilized protein. Triton shows the pattern of a segregating surfactant in the presence of cholesterol. Zeta potential measurements of liposomes exposed to surfactin show strong peptide-peptide interactions already at a few mol-% in the membrane.

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Protection Against Photodamage of Biological Membranes: Effectiveness of Gallic Acid on Model Lipid Bilayers

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Biological membranes contain a large amount of unsaturated lipids which may be easily degraded by action of singlet oxygen and free radicals generated by degradation of molecules exposed to light irradiation. Lipid peroxidation leads to changes in lipid bilayer permeability, fluidity and packing order [1]. In biological media, such effects accelerate cell aging and culminate in cell death. Methylene blue (MB) is a powerful oxidizing agent due to a high quantum yield of singlet oxygen production when exposed to light of appropriate wavelength [2]. On the other hand, gallic acid (GA) interacts physically and chemically with singlet oxygen [3]. In this work we evaluate the ability of GA in reducing the damage of mimetic biological membranes caused by the action of MB exposed to light irradiation. By means of phase contrast microscopy, it was possible to determine the best GA concentration to reduce the physical damage of the phospholipidic membrane of giant unilamellar vesicles and delay the permeability increase of the same. Furthermore, submitting the vesicles under adequate electric field [4], the increase of area per lipid as a result of oxidation promoted by irradiated MB was quantitatively determined in the absence and presence of different concentrations of GA. Results show a promising effect of GA in protecting against photo damage of biological membranes.

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Combined Brewster Angle and Fluorescence Microscopy of DMPC/D-Cholesterol Mixed Langmuir Monolayers

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Most direct imaging studies of domains and of the mixing/demixing transition within lipid monolayers and bilayers are performed with fluorescence microscopy (FM). This technique requires the addition of a fluorescent probe, which can in principle affect the size, shape and behavior of the domains, as well as